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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,104	08/17/2000	Walter Birchmeier	0107-028P	5225

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/641,104	Applicant(s) BIRCHMEIER ET AL.	
	Examiner Chih-Min Kam	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *9-19 and 29-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because the oath is not dated by the inventors, Walter Birchmeier and Jens-Peter Von Kries.

Election/Restrictions

2. Applicant's election with traverse of Group V, claims 1-8, 20-28 and SEQ ID NO:6 (arm 3) in Paper Nos. 13 and 16 is acknowledged. The traversal is on the ground(s) that the 7 sequences recited in Table 1 (armadillo peptides 3-9) belong together because they are representative of the single peptide, that of the human β-catenin. The argument is persuasive, thus, all 7 peptides (SEQ ID NOS: 6, 7, 8, 9, 10, 11 and 12) along with claims 1-8 and 20-28 are examined. The requirement is still deemed proper and is therefore made FINAL.

Abstract

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Informalities

The disclosure is objected to because of the following informalities:

4. The specification is objected to for not conforming C.F.R.37 1.822 (d)(1) since the amino acids in the peptide sequences of the invention are listed with one letter abbreviation instead of the required three- letter abbreviation with the first letter as an upper case character. Amino acid

sequences are cited, for example, at page 3 and Table 1, however, the sequence identifier "SEQ ID NO:" is not given. Appropriate correction is required.

5. The drawings (Figs. 1-6) and Tables 1-2 are described in German instead of English. Appropriate correction is required. Applicants also submit Tables 3 and 4 as part of specification, however, there is no description on Tables 3 and 4, and appropriate clarification is required.

6. At page 11, in the description of Fig. 2, the word "analine" is misspelled. Appropriate correction is required.

Claim Objections

7. Claim 20 is objected to because the claim recites Table 1 for the amino acid sequences of armadillo domain of β-catenin. For various amino acid sequences, the sequence identifier "SEQ ID NO:" instead of Table 1 should be cited in the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8 and 20-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for armadillo domains of β-catenin (arms 3-8) as an agent which affect the interaction between β-catenin and LEF-1/TCF-4 (transcription factor), or between β-catenin and APC or conductin (tumor suppressor gene product); or the mutants of these armadillo domains of β-catenin (arms 3-8) which have residue 253, 274, 338, 383, 469 or 470 substituted by Ala, does not reasonably provide enablement for an agent which affects the

interaction between β-catenin and a transcription factor, or between β-catenin and a tumor suppressor gene product; or a peptide which is a similar compound, a mutant or a fragment of an armadillo domain of β-catenin (arms 3-9). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-8 and 20-28 encompass any agent which affects the interaction between β-catenin and a transcription factor, or between β-catenin and a tumor suppressor gene product (claims 1-8); or a peptide which is a similar compound, a mutant or a fragment of an armadillo domain of β-catenin (claims 20-28). The specification, however, only discloses cursory conclusions (pages 1 and 3) without data supporting the findings, which states that the invention relates to agents for treating human illness such as cancers based on the agents which can affect the interaction between β-catenin and transcription factors or tumor suppressor gene products, and these agents can be peptides derived from β-catenin or similar compounds. There are no indicia that the present application enables the full scope in view of armadillo domains of β-catenin as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the agents affecting the interaction between β-catenin and a transcription factor, or between β-catenin and a tumor suppressor gene product, or peptides or similar compounds derived from armadillo domains of β-catenin, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed variants except for the armadillo domains of β-catenin (arms 3-9) and the specific mutants of these armadillo domains.

(3). The state of the prior art and relative skill of those in the art:

The prior art (WO 98/42296) indicates compounds that interact with stabilized β-catenin or LEF can be identified through the determination of the binding regions of β-catenin or LEF by experimentation or molecular modeling, however, such compounds have not been specified. The general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of various agents including the peptides, the fragments and mutants of armadillo domains of β-catenin to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass agents which affect the interaction between β-catenin and a transcription factor or a tumor suppressor gene product, the invention is highly unpredictable regarding the structures and the effects of these agents.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to agents which affect the interaction between β-catenin and a transcription factor or a tumor suppressor gene product; or a peptide, which is a similar compound, a mutant or a fragment of an armadillo domain of β-catenin. The specification indicates some basic (Lys, Arg, His) or some aromatic amino acids in the armadillo repeat units 3-9 of β-catenin can be mutated (pages 6-7; Fig. 5), and several critical amino acid residues of β-catenin which affect the interaction with LEF-1/TCF, APC, conductin or E-cadherin are identified (Figs 5 and 6; Table 2). However, the specification fails to identify any other compounds besides the armadillo repeat units 3-9 of β-catenin. Moreover, the specification has not shown any other compounds with different structures can affect the interaction between β-catenin and a transcription factor or a tumor suppressor gene product. There are no working examples indicating similar compounds, undefined mutants or fragments of armadillo domains of β-catenin can affect the interaction between β-catenin and a transcription factor or a tumor suppressor gene product. Furthermore, the specification does not provide any specific guidance on how to identify functional peptides, which have different structures from the armadillo repeat units 3-9 of β-catenin. Since the specification fails to provide sufficient guidance, it is necessary to carry out further experimentation to assess the effects of various compounds including the mutants or fragments derived from armadillo domains of β-catenin.

(6). Nature of the Invention

The scope of the claims encompasses agents with undefined structures including the peptides, which are similar compounds, mutants or fragments of armadillo domains of β-catenin, however, the specification does not show how to identify various agents besides the armadillo domains of β-catenin. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the art is unpredictable regarding the claimed variants, and the guidance and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the agents or the peptides or similar compounds of armadillo domains of β-catenin.

9. Claims 21 23, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21 23, 25 and 27 are directed to peptides containing the binding regions of β-catenin for LEF-1/TCF, APC 15 amino acid or 20 amino acid repeats, or conductin, and, the fragments of the peptides. The specification indicates that some basic (Lys, Arg, His) and some aromatic amino acids in the armadillo repeat units 3-9 of β-catenin were mutated (pages 6-7; Fig. 5), the mutant β-catenin were tested if they interact with LEF-1/TCF, APC, conductin or E-cadherin (Table 2), and several critical amino acid residues of β-catenin were identified (Figs. 5 and 6). However, the specification does not specify which portion of the armadillo repeat units 3-9 of β-catenin are included in the fragments. There is no disclosure indicating all the

fragments of the armadillo repeat units 3-9 are functional. Without guidance on structure to function/activity of the fragments, one skilled in the art would not know which region or residue of the fragment is essential for function/activity and how to identify a functional peptide. The lack of a structure to function/activity relationship and the lack of representative species for the fragments as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, for example, is indefinite because of the use of the terms "Agents for treating human illness based on substances" and "between β-catenin and transcription factors and tumor suppressor gene products". The terms "Agents for treating human illness based on substances" and "between β-catenin and transcription factors and tumor suppressor gene products" render the claim indefinite, it is unclear whether agents are compositions or compounds, whether the "substances" are the same as agents, what human illness is, and whether the substances also affect the interaction between β-catenin and tumor suppressor gene products. The use of the terms "An agent" and "between β-catenin and transcription factors or tumor suppressor gene

products" is suggested. See also claims 2 and 3. Claims 4-8 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

11. Claim 6 is indefinite because of the use of the term "AP 20 amino acid repeats". The term "AP 20 amino acid repeats" renders the claim indefinite, it is unclear what AP 20 amino acid repeats are.

12. Claims 20-22 and 24-28 are indefinite because of the use of the terms "similar molecules" and "mutants". The terms "similar molecules" and "mutants" render the claim indefinite, it is unclear what "similar molecules" are, and how much similarity exists between the similar molecules and the armadillo domain of β-catenin, and what amino acid sequences the mutants have, e.g., which amino acid residues are mutated, and what amino acid residues are used for mutation. Claims 21, 22 and 24-28 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

13. Claims 21-28 are indefinite because the claim recites amino acid position(s) without reference to a "SEQ ID NO:". It is not clear what the amino acid position is without a sequence identifier "SEQ ID NO:".

14. Claim 21, for example, is indefinite because of the use of the term "fragments". The term "fragments" renders the claim indefinite, it is unclear what amino acid sequence the fragment has, and whether the fragments contain His 470 or Arg 469. See also claims 23, 25 and 27.

15. Claims 21 and 22 are indefinite because of the use of the term "and/or". The term "and/or" renders the claim indefinite, it is unclear whether the item after "and/or" is included or not, and if included is to be read as an alternative "or" or the conjunctive "and".

16. Claim 22, for example, is indefinite because of the use of the term "mutation His 470 and/or Arg 469". The term "mutation His 470 and/or Arg 469" renders the claim indefinite, it is unclear which amino acid residue is used for mutation at position 469 or 470. See also claims 24, 26 and 28.

17. Claim 23 is indefinite because of the use of the term "20 mino acid repeats". The term "20 mino acid repeats" renders the claim indefinite, it is unclear what the term means.

Conclusion

18. No claims are allowed.

Art of Record

The following reference appears to be the closest art to the claimed invention. Polaskis *et al.* (WO 98/42296) teach compounds that interact with mutant stabilized β-catenin and/or LEF can be identified through the determination of the binding regions of β-catenin or LEF by experimentation or molecular modeling, however, such compounds have not been specified. It appears the armadillo peptides of β-catenin (SEQ ID NOs: 6, 7, 8, 9, 10, 11 and 12) are free of prior art as agents which affect the interaction the interaction between β-catenin and LEF-1/TCF-4 (transcription factor), or between β-catenin and APC or conductin (tumor suppressor gene product).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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August 19, 2002

GABRIELLE BUGAISKY
PRIMARY EXAMINER